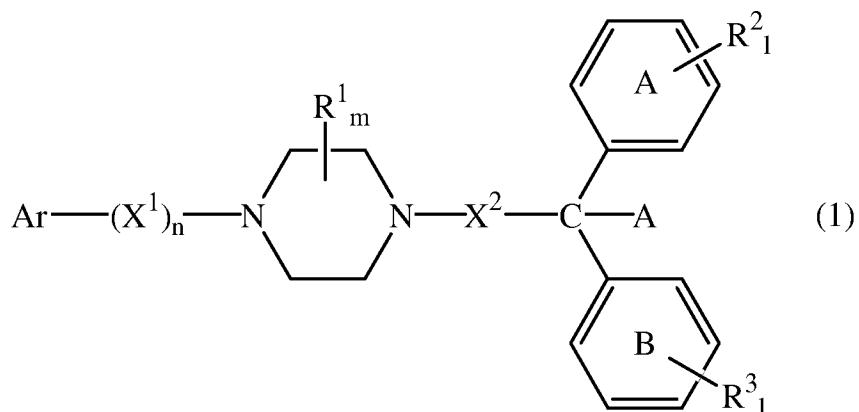


CLAIM AMENDMENTS

1. (currently amended): A method to treat pain which method comprises administering to a subject in need of such treatment an effective amount of a compound of the formula:



or a pharmaceutically acceptable salt thereof,

wherein Ar is phenyl, ~~a six membered or five membered ring which is heteroaromatic or a fused aromatic or heteroaromatic system~~ pyridyl, pyrimidyl, indolyl, benzimidazolyl, benzotriazolyl, isoquinolyl, quinolyl, benzothiazolyl, benzofuranyl, thienyl, furyl, pyrrolyl, thiazolyl, oxazolyl, imidazolyl or phthalimido, each of which may optionally be substituted with one or more ~~non interfering substituents~~ alkyl (1-10C), alkenyl (2-10C), alkynyl (2-10C), aryl (6-10C), arylalkyl (1-16C), arylalkenyl (7-16C), each optionally containing 1-4 heteroatoms (N, O or S), O-aryl, O-alkylaryl, O-aroyl, NR-aryl, N-alkylaryl, NR-aroyl, halo, OR, NR₂, SR, -OOCR, -NROCR, RCO, -COOR, -CONR₂, and/or SO₂NR₂, wherein each R is independently H or alkyl (1-8C), and/or by -CN, OCF, -CF₃, and/or NO₂;

~~X¹ is a linker containing 1-5 members~~ 1-5 member chain linking the piperazine to Ar;

n is 1;

~~each R¹-R³ is independently a non interfering non hydrogen substituent~~ alkyl (1-10C), alkenyl (2-10C), alkynyl (2-10C), aryl (6-10C), arylalkyl (1-16C), arylalkenyl (7-16C), each optionally containing 1-4 heteroatoms (N, O or S), O-aryl, O-alkylaryl, O-aroyl, NR-aryl, N-alkylaryl, NR-aroyl, halo, OR, NR₂, SR, -OOCR, -NROCR, RCO, -COOR, -CONR₂, and/or

SO₂NR₂, wherein each R is independently H or alkyl (1-8C), and/or by -CN, OCF, -CF₃, and/or NO₂;

each 1 is independently 0-5;

m is 0-4;

X² is a linker comprising a chain of at least 5 members;

A is H, OR, SR, NR₂, or halo wherein R is H or lower alkyl (1-6C);

with the proviso that

(a) Ar is a five or six membered heteroaryl substituent or an optionally substituted fused aromatic or heteroaromatic substituent pyridyl, pyrimidyl, indolyl, benzimidazolyl, benzotriazolyl, isoquinolyl, quinolyl, benzothiazolyl, benzofuranyl, thienyl, furyl, pyrrolyl, thiazolyl, oxazolyl, imidazolyl or phthalimido optionally substituted with one or more of alkyl (1-10C), alkenyl (2-10C), alkynyl (2-10C), aryl (6-10C), arylalkyl (1-16C), arylalkenyl (7-16C), each optionally containing 1-4 heteroatoms (N, O or S), O-aryl, O-alkylaryl, O-acyl, NR-aryl, N-alkylaryl, NR-acyl, halo, OR, NR₂, SR, -OOCR, -NROCR, RCO, -COOR, -CONR₂, and/or SO₂NR₂, wherein each R is independently H or alkyl (1-8C), and/or by -CN, OCF, -CF₃, and/or NO₂; and/or

(b) m is 1-4; and/or

(c) X² is alkylene substituted by =O, OR, SR, NR₂ and/or halo; and/or

(d) X² is a chain of at least 6 members; and/or

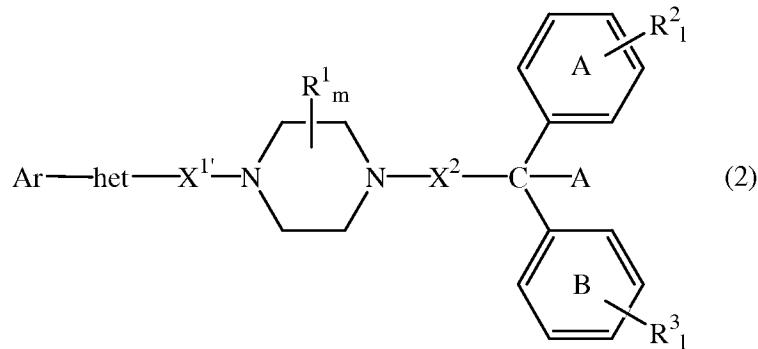
(e) X² contains at least one heteroatom selected from N, S and O; and/or

(f) A is OR, SR, NR₂ or halo, wherein R is H or lower alkyl (1-6C) and/or

(g) Ar is substituted with at least one t-butyl moiety or at least one substituted alkoxy; and/or

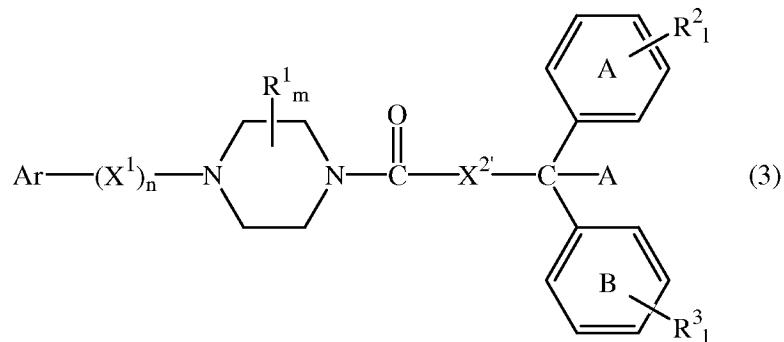
(h) X¹ includes at least one heteroatom selected from O, N and S.

2. (previously presented): The method of claim 1 wherein the compound of formula (1) is of the formula



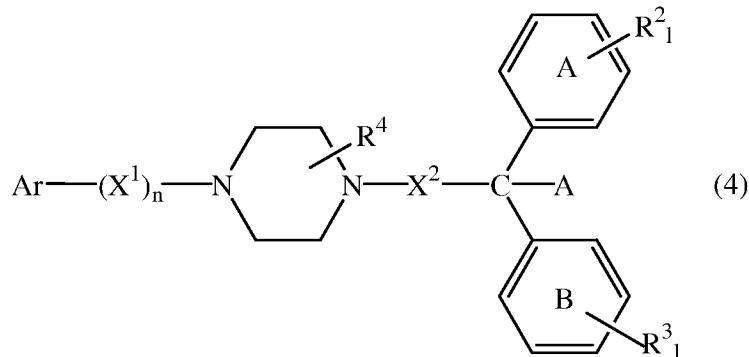
wherein Ar, R¹-R³, l, m, X² and A are as defined above, “het” is a heteroatom selected from O, S and N, and wherein X^{1'} is defined as X¹ but lacking one chain member.

3. (previously presented): The method of claim 1 wherein the compound of formula (1) is of the formula



wherein Ar, X¹, R¹-R³, l, m, n, A and Ar are defined as above, and X^{2'} is defined as X² but lacking one chain member.

4. (previously presented): The method of claim 1 wherein the compound of formula (1) is of the formula



wherein R^4 is $=O$, or a carboxylic acid group or ester or amide thereof and Ar , R^2-R^3 , X^1 , n , X^2 and A are defined as above.

5. (currently amended): The method of claim 1, wherein each R^1-R^3 and optional Ar ~~non-interfering~~ substituent is independently alkyl (1-10C), alkenyl (2-10C), alkynyl (2-10C), aryl (6-10C), arylalkyl (7-16C) or arylalkenyl (7-16C) each optionally further containing 1-4 heteroatoms (N, O or S), or is each further optionally substituted, or is independently $=O$, halo, CF_3 , OCF , NO_2 , NH_2 , OH , or SH wherein S may optionally be oxidized.

6. (canceled)

7. (previously presented): The method of claim 1, wherein each l is independently 0 or 1.

8. (canceled)

9. (previously presented): The method of claim 1, wherein X^1 is substituted by $=O$ at the position next to the piperazine ring.

10. (previously presented): The method of claim 1, wherein each of R^2 and R^3 is independently alkoxy, halo, or alkyl.

11. (previously presented): The method of claim 1, wherein m is 1 and R¹ is =O or a is carboxylic acid group or ester or amide thereof.

12. (previously presented): The method of claim 1, wherein Ar is optionally substituted phenyl.

13. (previously presented): The method of claim 12, wherein said phenyl is unsubstituted or is substituted by one or more tert-butyl, methoxy, substituted alkoxy, hydroxy and/or halo.

14. (previously presented): The method of claim 13, wherein the substituted alkoxy is substituted by an amino group.

15. (previously presented): The method of claim 1, wherein Ar is optionally substituted pyrimidyl, pyridyl, benzothiazole, benzimidazole or indole.

16. (previously presented): A method to treat pain which method comprises administering to a subject in need of such treatment an effective amount of a compound selected from the group consisting of

6,6-Bis-(4-fluoro-phenyl)-1-[4-(2-phenylsulfanyl-ethyl)-piperazin-1-yl]-hexan-1-one;
1-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-4-[2-(4-fluoro-phenoxy)-ethyl]-piperazine;
1-{4-[2-(Benzo[1,3]dioxol-5-yloxy)-ethyl]-piperazin-1-yl}-6,6-bis-(4-fluoro-phenyl)-hexan-1-one;

1-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-4-(2-phenylsulfanyl-ethyl)-piperazine;
1-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-4-[2-(4-methoxy-phenoxy)-ethyl]-piperazine;
1-{4-[2-(2,4-Difluoro-phenoxy)-ethyl]-piperazin-1-yl}-6,6-bis-(4-fluoro-phenyl)-hexan-1-one;

6,6-Bis-(4-fluoro-phenyl)-1-[4-(2-phenoxy-ethyl)-piperazin-1-yl]-hexan-1-one;
1-{4-[2-(2,4-Dichloro-phenoxy)-ethyl]-piperazin-1-yl}-6,6-bis-(4-fluoro-phenyl)-hexan-1-one;

6,6-Bis-(4-fluoro-phenyl)-1-{4-[2-(4-methoxy-phenoxy)-ethyl]-piperazin-1-yl}-hexan-1-one;

1-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-4-(2-phenoxy-ethyl)-piperazine;

6,6-Bis-(4-fluoro-phenyl)-1-{4-[2-(3,4,5-trimethoxy-phenoxy)-ethyl]-piperazin-1-yl}-hexan-1-one;

1-{4-[2-(Benzothiazol-2-ylsulfanyl)-ethyl]-piperazin-1-yl}-6,6-bis-(4-fluoro-phenyl)-hexan-1-one;

[4-(2-{4-[6,6-Bis-(4-fluoro-phenyl)-hexanoyl]-piperazin-1-yl}-ethoxy)-2,3,6-trimethyl-phenyl]-carbamic acid tert-butyl ester;

4-(2-{4-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-piperazin-1-yl}-ethoxy)-2,3,6-trimethyl-phenylamine;

1-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-4-[2-(2,4-dichloro-phenoxy)-ethyl]-piperazine;

[2-(4-{4-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-piperazin-1-ylmethyl}-2,6-di-tert-butyl-phenoxy)-ethyl]-dimethyl-amine;

4-{4-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-piperazin-1-ylmethyl}-2,6-di-tert-butyl-phenol;

1-[4-(3,5-Di-tert-butyl-4-methoxy-benzoyl)-piperazin-1-yl]-6,6-bis-(4-fluoro-phenyl)-hexan-1-one;

1-[4-(3,5-Di-tert-butyl-4-methoxy-benzyl)-piperazin-1-yl]-6,6-bis-(4-fluoro-phenyl)-hexan-1-one;

1-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-4-(3,5-di-tert-butyl-4-methoxy-benzyl)-piperazine;

{4-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-piperazin-1-yl}-(3,5-di-tert-butyl-4-methoxy-phenyl)-methanone;

1-{4-[3,5-Di-tert-butyl-4-(2-dimethylamino-ethoxy)-benzoyl]-piperazin-1-yl}-6,6-bis-(4-fluoro-phenyl)-hexan-1-one;

1-Benzo[1,3]dioxol-5-ylmethyl-4-[6,6-bis-(4-fluoro-phenyl)-hexyl]-piperazine;

1-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-4-(3,5-di-tert-butyl-benzyl)-piperazine;

{4-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-piperazin-1-yl}-(3,5-di-tert-butyl-4-hydroxy-phenyl)-methanone;

1-[4-(3,5-Di-tert-butyl-4-hydroxy-benzyl)-piperazin-1-yl]-6,6-bis-(4-fluoro-phenyl)-hexan-1-one;

1-[4-(3,5-Dibromo-4-hydroxy-benzoyl)-piperazin-1-yl]-6,6-bis-(4-fluoro-phenyl)-hexan-1-one;

1-[4-(3,5-Di-tert-butyl-4-hydroxy-benzoyl)-piperazin-1-yl]-6,6-bis-(4-fluoro-phenyl)-hexan-1-one;

1-[4-(3,5-Di-tert-butyl-benzoyl)-piperazin-1-yl]-6,6-bis-(4-fluoro-phenyl)-hexan-1-one;

1-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-4-(4-tert-butyl-benzyl)-piperazine;

1-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-4-(9H-thioxanthen-9-yl)-piperazine;

2-{4-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-piperazin-1-yl}-benzothiazole;

6,6-Bis-(4-fluoro-phenyl)-1-(4-pyrimidin-2-yl-piperazin-1-yl)-hexan-1-one;

2-{4-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-piperazin-1-yl}-pyrimidine;

6,6-Bis-(4-fluoro-phenyl)-1-[4-(9H-thioxanthen-9-yl)-piperazin-1-yl]-hexan-1-one;

1-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-4-(3,4,5-trimethoxy-benzyl)-piperazine-2-carboxylic acid ethyl ester;

6,6-Bis-(4-fluoro-phenyl)-1-{4-[2-(3,4,5-trimethoxy-benzylamino)-ethyl]-piperazin-1-yl}-hexan-1-one;

9,9-Bis-(4-fluoro-phenyl)-1-[4-(3,4,5-trimethoxy-benzyl)-piperazin-1-yl]-nonan-1-one;

(2-{4-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-piperazin-1-yl}-ethyl)-phenyl-amine;

1-[9,9-Bis-(4-fluoro-phenyl)-nonyl]-4-(3,4,5-trimethoxy-benzyl)-piperazine;

(4-{4-[Bis-(4-fluoro-phenyl)-methoxy]-butyl}-piperazin-1-yl)-(3,4,5-trimethoxy-phenyl)-methanone;

6,6-Bis-(4-fluoro-phenyl)-1-[4-(4-trifluoromethoxy-benzoyl)-piperazin-1-yl]-hexan-2-one;

1-[4-(4-Bromo-benzoyl)-piperazin-1-yl]-6,6-bis-(4-fluoro-phenyl)-hexan-1-one;

6,6-Bis-(4-fluoro-phenyl)-5-hydroxy-1-[4-(3,4,5-trimethoxy-benzoyl)-piperazin-1-yl]-hexan-1-one;

1-{4-[Bis-(4-fluoro-phenyl)-methoxy]-butyl}-4-(3,4,5-trimethoxy-benzyl)-piperazine;

6,6-Bis-(4-fluoro-phenyl)-6-hydroxy-1-[4-(3,4,5-trimethoxy-benzoyl)-piperazin-1-yl]-hexan-1-one;

4-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-1-(3,4,5-trimethoxy-benzyl)-piperazine-2-carboxylic acid;

4-[6,6-Bis-(4-fluoro-phenyl)-hexanoyl]-1-(3,4,5-trimethoxy-benzyl)-piperazin-2-one;

1-[6,6-Bis-(4-fluoro-phenyl)-hexanoyl]-4-(3,5-di-tert-butyl-4-methoxy-benzoyl)-piperazin-2-one;

1-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-4-(3,4,5-trimethoxy-benzoyl)-piperazin-2-one;

4-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-1-(3,4,5-trimethoxy-benzyl)-piperazin-2-one;

4-[6,6-Bis-(4-fluoro-phenyl)-hexanoyl]-1-(3,5-di-tert-butyl-4-methoxy-benzoyl)-piperazin-2-one;

4-[6,6-Bis-(4-fluoro-phenyl)-hexanoyl]-1-[2-(4-fluoro-phenoxy)-ethyl]-piperazin-2-one;

1-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-4-(3,5-di-tert-butyl-4-methoxy-benzoyl)-piperazin-2-one;

4-[6,6-Bis-(4-fluoro-phenyl)-hexanoyl]-1-(3,5-di-tert-butyl-4-methoxy-benzoyl)-piperazin-2-one;

1-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-4-(3,5-di-tert-butyl-4-hydroxy-benzoyl)-piperazin-2-one;

1-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-4-(3,5-di-tert-butyl-4-hydroxy-benzoyl)-piperazin-2-one;

6,6-Bis-(4-fluoro-phenyl)-1-[4-(3,4,5-trimethoxy-benzoyl)-piperazin-1-yl]-hex-5-en-1-one;

1-{4-[2-(3,4-Dimethoxy-phenoxy)-ethyl]-piperazin-1-yl}-6,6-bis-(4-fluoro-phenyl)-hexan-1-one;

1-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-4-[2-(3,4-dimethoxy-phenoxy)-ethyl]-piperazine;

1-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-4-(3,4,5-trimethoxy-benzyl)-piperazine-2-carboxylic acid ethyl ester;

1-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-4-(3,4-dimethoxy-benzyl)-piperazine;

1-[4-(3,4-Dimethoxy-benzoyl)-piperazin-1-yl]-6,6-bis-(4-fluoro-phenyl)-hexan-1-one;

1-[2-(Benzo[1,3]dioxol-5-yloxy)-ethyl]-4-[6,6-bis-(4-fluoro-phenyl)-hexyl]-piperazine;

1-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-4-[2-(3,4,5-trimethoxy-phenoxy)-ethyl]-piperazine;

1-(4-Amino-2,3,5-trimethyl-phenoxy)-3-{4-[6,6-bis-(4-fluoro-phenyl)-hexyl]-piperazin-1-yl}-propan-2-ol;

1-{4-[3-(4-Amino-2,3,5-trimethyl-phenoxy)-2-hydroxy-propyl]-piperazin-1-yl}-6,6-bis-(4-fluoro-phenyl)-hexan-1-one;

1-(4-Benzothiazol-2-yl-piperazin-1-yl)-6,6-bis-(4-fluoro-phenyl)-hexan-1-one;

1-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-4-(3,5-bis-trifluoromethyl-benzyl)-piperazine;

1-[4-(3,5-Bis-trifluoromethyl-benzoyl)-piperazin-1-yl]-6,6-bis-(4-fluoro-phenyl)-hexan-1-one;

1-[4-(4-tert-Butyl-benzoyl)-piperazin-1-yl]-6,6-bis-(4-fluoro-phenyl)-hexan-1-one;

1-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-4-(4-bromo-benzyl)-piperazine;

2-(2-{4-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-piperazin-1-yl}-ethylsulfanyl)-benzothiazole;

6,6-Bis-(4-fluoro-phenyl)-1-[4-(4-hydroxy-3,5-dimethoxy-benzoyl)-piperazin-1-yl]-hexan-1-one;

4-{4-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-piperazin-1-ylmethyl}-2,6-dibromo-phenol;

1-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-4-(4-trifluoromethoxy-benzyl)-piperazine;

(2-{4-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-piperazin-1-yl}-ethyl)-(3,4,5-trimethoxy-benzyl)-amine;

1-{4-[2-(4-Fluoro-phenoxy)-ethyl]-piperazin-1-yl}-6,6-bis-(4-fluoro-phenyl)-hexan-1-one;

6,6-Bis-(4-fluoro-phenyl)-1-[4-(2-phenylamino-ethyl)-piperazin-1-yl]-hexan-1-one;

1-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-4-[2-(2,4-difluoro-phenoxy)-ethyl]-piperazine;

N-(2-{4-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-piperazin-1-yl}-2-oxo-ethyl)-benzamide;

N-(2-{4-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-piperazin-1-yl}-2-oxo-ethyl)-4-chloro-benzamide;

N-(2-{4-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-piperazin-1-yl}-2-oxo-ethyl)-4-methyl-benzamide;

N-(2-{4-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-piperazin-1-yl}-2-oxo-ethyl)-4-isopropyl-benzamide;

N-(2-{4-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-piperazin-1-yl}-2-oxo-ethyl)-4-tert-butyl-benzamide;

N-(2-{4-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-piperazin-1-yl}-2-oxo-ethyl)-4-fluoro-benzamide;

N-(2-{4-[6,6-Bis-(4-fluoro-phenyl)-hexanoyl]-piperazin-1-yl}-2-oxo-ethyl)-benzamide;

N-(2-{4-[6,6-Bis-(4-fluoro-phenyl)-hexanoyl]-piperazin-1-yl}-2-oxo-ethyl)-4-chloro-benzamide;

N-(2-{4-[6,6-Bis-(4-fluoro-phenyl)-hexanoyl]-piperazin-1-yl}-2-oxo-ethyl)-4-methyl-benzamide;

N-(2-{4-[6,6-Bis-(4-fluoro-phenyl)-hexanoyl]-piperazin-1-yl}-2-oxo-ethyl)-4-isopropyl-benzamide;

N-(2-{4-[6,6-Bis-(4-fluoro-phenyl)-hexanoyl]-piperazin-1-yl}-2-oxo-ethyl)-4-tert-butyl-benzamide;

N-(2-{4-[6,6-Bis-(4-fluoro-phenyl)-hexanoyl]-piperazin-1-yl}-2-oxo-ethyl)-4-fluoro-benzamide;

1-[4-(2-Benzylamino-ethyl)-piperazin-1-yl]-6,6-bis-(4-fluoro-phenyl)-hexan-1-one;

1-{4-[2-(4-Chloro-benzylamino)-ethyl]-piperazin-1-yl}-6,6-bis-(4-fluoro-phenyl)-hexan-1-one;

6,6-Bis-(4-fluoro-phenyl)-1-{4-[2-(4-methyl-benzylamino)-ethyl]-piperazin-1-yl}-hexan-1-one;

6,6-Bis-(4-fluoro-phenyl)-1-{4-[2-(4-isopropyl-benzylamino)-ethyl]-piperazin-1-yl}-hexan-1-one;

1-{4-[2-(4-tert-Butyl-benzylamino)-ethyl]-piperazin-1-yl}-6,6-bis-(4-fluoro-phenyl)-hexan-1-one;

1-{4-[2-(4-Fluoro-benzylamino)-ethyl]-piperazin-1-yl}-6,6-bis-(4-fluoro-phenyl)-hexan-1-one;

6,6-Bis-(4-fluoro-phenyl)-1-[4-(1-hydroxy-pyridine-4-carbonyl)-piperazin-1-yl]-hexan-1-one;

4-{4-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-piperazin-1-ylmethyl}-2,6-dimethoxy-phenol;

9,9-Diphenyl-1-[4-(3,4,5-trimethoxy-benzyl)-piperazin-1-yl]-nonan-1-one;

1-[4-(3,5-Di-tert-butyl-4-methoxy-benzoyl)-2-methyl-piperazin-1-yl]-6,6-bis-(4-fluoro-phenyl)-hexan-1-one;

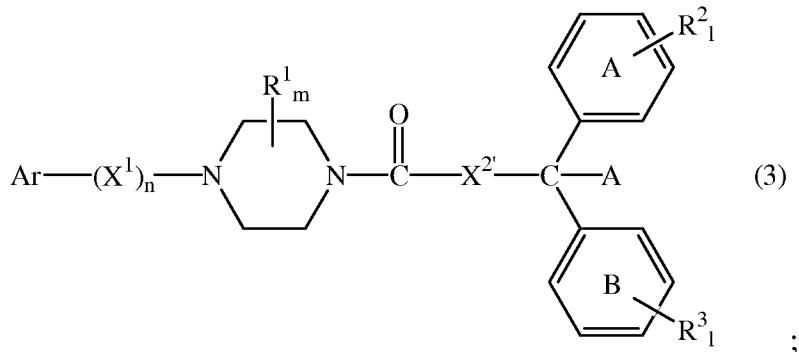
1-[4-(3,5-Di-tert-butyl-4-methoxy-benzoyl)-3-methyl-piperazin-1-yl]-6,6-bis-(4-fluoro-phenyl)-hexan-1-one;

1-[4-(3,5-Di-tert-butyl-benzoyl)-2-methyl-piperazin-1-yl]-6,6-bis-(4-fluoro-phenyl)-hexan-1-one; and

1-[4-(4-tert-Butyl-benzoyl)-2-methyl-piperazin-1-yl]-6,6-bis-(4-fluoro-phenyl)-hexan-1-one, including the pharmaceutically acceptable salts thereof.

17-18. (canceled)

19. (currently amended): A compound of the formula



wherein Ar is phenyl, a six membered or five membered ring which is heteroaromatic or a fused aromatic or heteroaromatic system pyridyl, pyrimidyl, indolyl, benzimidazolyl, benzotriazolyl, isoquinolyl, quinolyl, benzothiazolyl, benzofuranyl, thienyl, furyl, pyrrolyl, thiazolyl, oxazolyl, imidazolyl or phthalimido, each of which may optionally be substituted with one or more non-interfering substituents alkyl (1-10C), alkenyl (2-10C), alkynyl (2-10C), aryl (6-10C), arylalkyl (1-16C), arylalkenyl (7-16C), each optionally containing 1-4 heteroatoms (N, O or S), O-aryl, O-alkylaryl, O-aroyl, NR-aryl, N-alkylaryl, NR-aroyl, halo, OR, NR₂, SR, -OOCR, -NROCR, RCO, -COOR, -CONR₂, and/or SO₂NR₂, wherein each R is independently H or alkyl (1-8C), and/or by -CN, OCF, -CF₃, and/or NO₂;

X¹ is a linker containing 1-5 members 1-5 member chain linking the piperazine to Ar;

n is 1;

each R¹-R³ is independently a non-interfering non-hydrogen substituent alkyl (1-10C), alkenyl (2-10C), alkynyl (2-10C), aryl (6-10C), arylalkyl (1-16C), arylalkenyl (7-16C), each optionally containing 1-4 heteroatoms (N, O or S), O-aryl, O-alkylaryl, O-aroyl, NR-aryl, N-alkylaryl, NR-aroyl, halo, OR, NR₂, SR, -OOCR, -NROCR, RCO, -COOR, -CONR₂, and/or SO₂NR₂, wherein each R is independently H or alkyl (1-8C), and/or by -CN, OCF, -CF₃, and/or NO₂;

each l is independently 0-5;

m is 0-4;

X^{2'} is a linker comprising a chain of at least 4 members;

A is H, OR, SR, NR₂, or halo wherein R is H or lower alkyl (1-6C);

with the proviso that

(a) Ar is a five or six membered heteroaryl substituent or an optionally substituted fused aromatic or heteroaromatic substituent pyridyl, pyrimidyl, indolyl, benzimidazolyl, benzotriazolyl, isoquinolyl, quinolyl, benzothiazolyl, benzofuranyl, thienyl, furyl, pyrrolyl, thiazolyl, oxazolyl, imidazolyl or phthalimido optionally substituted with one or more of alkyl (1-10C), alkenyl (2-10C), alkynyl (2-10C), aryl (6-10C), arylalkyl (1-16C), arylalkenyl (7-16C), each optionally containing 1-4 heteroatoms (N, O or S), O-aryl, O-alkylaryl, O-aroyl, NR-aryl, N-alkylaryl, NR-aroyl, halo, OR, NR₂, SR, -OOCR, -NROCR, RCO, -COOR, -CONR₂, and/or SO₂NR₂, wherein each R is independently H or alkyl (1-8C), and/or by -CN, OCF, -CF₃, and/or NO₂; and/or

(b) m is 1-4; and/or

(c) X² is alkylene substituted by =O, OR, SR, NR₂ and/or halo; and/or

(d) X² is a chain of at least 6 members; and/or

(e) X² contains at least one heteroatom selected from N, S and O; and/or

(f) A is OR, SR, NR₂ or halo, wherein R is H or lower alkyl (1-6C) and/or

(g) Ar is substituted with at least one t-butyl moiety or at least one substituted alkoxy; and/or

(h) X¹ includes at least one heteroatom selected from O, N and S.

20. (currently amended): The compound of claim 19, wherein each R¹-R³ and optional Ar non-interfering substituent is independently alkyl (1-10C), alkenyl (2-10C), alkynyl (2-10C), aryl (6-10C), arylalkyl (7-16C) or arylalkenyl (7-16C) each optionally further containing 1-4 heteroatoms (N, O or S)-each further optionally substituted, or is independently [[=O]], halo, CF₃, OCF, NO₂, NH₂, OH, or SH wherein S may optionally be oxidized.

21. (previously presented): The compound of claim 19, wherein each l is independently 0 or 1.

22. (previously presented): The compound of claim 19, wherein X¹ is substituted by =O at the position next to the piperazine ring.

23. (previously presented): The compound of claim 19, wherein each of R² and R³ is independently alkoxy, halo, or alkyl.

24. (previously presented): The compound of claim 19, wherein m is 1 and R¹ is =O or a carboxylic acid group or ester or amide thereof.

25. (previously presented): The compound of claim 19, wherein Ar is optionally substituted phenyl.

26. (previously presented): The compound of claim 25, wherein said phenyl is unsubstituted or is substituted by one or more tert-butyl, methoxy, substituted alkoxy, hydroxy and/or halo.

27. (previously presented): The compound of claim 26, wherein the substituted alkoxy is substituted by an amino group.

28. (previously presented): The compound of claim 19, wherein Ar is optionally substituted pyrimidyl, pyridyl, benzothiazole, benzimidazole or indole.

29. (previously presented): A compound selected from the group consisting of
6,6-Bis-(4-fluoro-phenyl)-1-[4-(2-phenylsulfanyl-ethyl)-piperazin-1-yl]-hexan-1-one;
1-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-4-[2-(4-fluoro-phenoxy)-ethyl]-piperazine;
1-{4-[2-(Benzo[1,3]dioxol-5-yloxy)-ethyl]-piperazin-1-yl}-6,6-bis-(4-fluoro-phenyl)-
hexan-1-one;
1-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-4-(2-phenylsulfanyl-ethyl)-piperazine;
1-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-4-[2-(4-methoxy-phenoxy)-ethyl]-piperazine;
1-{4-[2-(2,4-Difluoro-phenoxy)-ethyl]-piperazin-1-yl}-6,6-bis-(4-fluoro-phenyl)-
hexan-1-one;
6,6-Bis-(4-fluoro-phenyl)-1-[4-(2-phenoxy-ethyl)-piperazin-1-yl]-hexan-1-one;
1-{4-[2-(2,4-Dichloro-phenoxy)-ethyl]-piperazin-1-yl}-6,6-bis-(4-fluoro-phenyl)-
hexan-1-one;
6,6-Bis-(4-fluoro-phenyl)-1-{4-[2-(4-methoxy-phenoxy)-ethyl]-piperazin-1-yl}-
hexan-1-one;
1-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-4-(2-phenoxy-ethyl)-piperazine;
6,6-Bis-(4-fluoro-phenyl)-1-{4-[2-(3,4,5-trimethoxy-phenoxy)-ethyl]-piperazin-1-yl}-
hexan-1-one;
1-{4-[2-(Benzothiazol-2-ylsulfanyl)-ethyl]-piperazin-1-yl}-6,6-bis-(4-fluoro-phenyl)-
hexan-1-one;
[4-(2-{4-[6,6-Bis-(4-fluoro-phenyl)-hexanoyl]-piperazin-1-yl}-ethoxy)-2,3,6-trimethyl-
phenyl]-carbamic acid tert-butyl ester;
4-(2-{4-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-piperazin-1-yl}-ethoxy)-2,3,6-trimethyl-
phenylamine;
1-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-4-[2-(2,4-dichloro-phenoxy)-ethyl]-piperazine;
[2-(4-{4-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-piperazin-1-ylmethyl}-2,6-di-tert-butyl-
phenoxy)-ethyl]-dimethyl-amine;
4-{4-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-piperazin-1-ylmethyl}-2,6-di-tert-butyl-phenol;
1-[4-(3,5-Di-tert-butyl-4-methoxy-benzoyl)-piperazin-1-yl]-6,6-bis-(4-fluoro-phenyl)-
hexan-1-one;

1-[4-(3,5-Di-tert-butyl-4-methoxy-benzyl)-piperazin-1-yl]-6,6-bis-(4-fluoro-phenyl)-hexan-1-one;

1-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-4-(3,5-di-tert-butyl-4-methoxy-benzyl)-piperazine;

{4-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-piperazin-1-yl}-(3,5-di-tert-butyl-4-methoxy-phenyl)-methanone;

1-{4-[3,5-Di-tert-butyl-4-(2-dimethylamino-ethoxy)-benzoyl]-piperazin-1-yl}-6,6-bis-(4-fluoro-phenyl)-hexan-1-one;

1-Benzo[1,3]dioxol-5-ylmethyl-4-[6,6-bis-(4-fluoro-phenyl)-hexyl]-piperazine;

1-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-4-(3,5-di-tert-butyl-benzyl)-piperazine;

{4-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-piperazin-1-yl}-(3,5-di-tert-butyl-4-hydroxy-phenyl)-methanone;

1-[4-(3,5-Di-tert-butyl-4-hydroxy-benzyl)-piperazin-1-yl]-6,6-bis-(4-fluoro-phenyl)-hexan-1-one;

1-[4-(3,5-Dibromo-4-hydroxy-benzoyl)-piperazin-1-yl]-6,6-bis-(4-fluoro-phenyl)-hexan-1-one;

1-[4-(3,5-Di-tert-butyl-4-hydroxy-benzoyl)-piperazin-1-yl]-6,6-bis-(4-fluoro-phenyl)-hexan-1-one;

1-[4-(3,5-Di-tert-butyl-benzoyl)-piperazin-1-yl]-6,6-bis-(4-fluoro-phenyl)-hexan-1-one;

1-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-4-(4-tert-butyl-benzyl)-piperazine;

1-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-4-(9H-thioxanthen-9-yl)-piperazine;

2-{4-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-piperazin-1-yl}-benzothiazole;

6,6-Bis-(4-fluoro-phenyl)-1-(4-pyrimidin-2-yl-piperazin-1-yl)-hexan-1-one;

2-{4-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-piperazin-1-yl}-pyrimidine;

6,6-Bis-(4-fluoro-phenyl)-1-[4-(9H-thioxanthen-9-yl)-piperazin-1-yl]-hexan-1-one;

1-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-4-(3,4,5-trimethoxy-benzyl)-piperazine-2-carboxylic acid ethyl ester;

6,6-Bis-(4-fluoro-phenyl)-1-{4-[2-(3,4,5-trimethoxy-benzylamino)-ethyl]-piperazin-1-yl}-hexan-1-one;

9,9-Bis-(4-fluoro-phenyl)-1-[4-(3,4,5-trimethoxy-benzyl)-piperazin-1-yl]-nonan-1-one;

(2-{4-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-piperazin-1-yl}-ethyl)-phenyl-amine;
1-[9,9-Bis-(4-fluoro-phenyl)-nonyl]-4-(3,4,5-trimethoxy-benzyl)-piperazine;
(4-{4-[Bis-(4-fluoro-phenyl)-methoxy]-butyl}-piperazin-1-yl)-(3,4,5-trimethoxy-phenyl)-
methanone;

6,6-Bis-(4-fluoro-phenyl)-1-[4-(4-trifluoromethoxy-benzoyl)-piperazin-1-yl]-hexan-2-one;
1-[4-(4-Bromo-benzoyl)-piperazin-1-yl]-6,6-bis-(4-fluoro-phenyl)-hexan-1-one;
6,6-Bis-(4-fluoro-phenyl)-5-hydroxy-1-[4-(3,4,5-trimethoxy-benzoyl)-piperazin-1-yl]-
hexan-1-one;

1-{4-[Bis-(4-fluoro-phenyl)-methoxy]-butyl}-4-(3,4,5-trimethoxy-benzyl)-piperazine;
6,6-Bis-(4-fluoro-phenyl)-6-hydroxy-1-[4-(3,4,5-trimethoxy-benzoyl)-piperazin-1-yl]-
hexan-1-one;

4-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-1-(3,4,5-trimethoxy-benzyl)-piperazine-2-
carboxylic acid;

4-[6,6-Bis-(4-fluoro-phenyl)-hexanoyl]-1-(3,4,5-trimethoxy-benzyl)-piperazin-2-one;
1-[6,6-Bis-(4-fluoro-phenyl)-hexanoyl]-4-(3,5-di-tert-butyl-4-methoxy-benzoyl)-
piperazin-2-one;

1-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-4-(3,4,5-trimethoxy-benzoyl)-piperazin-2-one;
4-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-1-(3,4,5-trimethoxy-benzyl)-piperazin-2-one;
4-[6,6-Bis-(4-fluoro-phenyl)-hexanoyl]-1-(3,5-di-tert-butyl-4-methoxy-benzyl)-
piperazin-2-one;

4-[6,6-Bis-(4-fluoro-phenyl)-hexanoyl]-1-[2-(4-fluoro-phenoxy)-ethyl]-piperazin-2-one;
1-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-4-(3,5-di-tert-butyl-4-methoxy-benzoyl)-
piperazin-2-one;

4-[6,6-Bis-(4-fluoro-phenyl)-hexanoyl]-1-(3,5-di-tert-butyl-4-methoxy-benzoyl)-
piperazin-2-one;

1-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-4-(3,5-di-tert-butyl-4-methoxy-benzyl)-piperazin-2-one;
1-[6,6-Bis-(4-fluoro-phenyl)-hexanoyl]-4-(3,5-di-tert-butyl-4-hydroxy-benzoyl)-
piperazin-2-one;

6,6-Bis-(4-fluoro-phenyl)-1-[4-(3,4,5-trimethoxy-benzoyl)-piperazin-1-yl]-hex-5-en-1-one;

1-[4-[2-(3,4-Dimethoxy-phenoxy)-ethyl]-piperazin-1-yl]-6,6-bis-(4-fluoro-phenyl)-hexan-1-one;

1-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-4-[2-(3,4-dimethoxy-phenoxy)-ethyl]-piperazine;

1-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-4-(3,4,5-trimethoxy-benzyl)-piperazine-2-carboxylic acid;

4-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-1-(3,4,5-trimethoxy-benzyl)-piperazine-2-carboxylic acid ethyl ester;

1-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-4-(3,4-dimethoxy-benzyl)-piperazine;

1-[4-(3,4-Dimethoxy-benzoyl)-piperazin-1-yl]-6,6-bis-(4-fluoro-phenyl)-hexan-1-one;

1-[2-(Benzo[1,3]dioxol-5-yloxy)-ethyl]-4-[6,6-bis-(4-fluoro-phenyl)-hexyl]-piperazine;

1-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-4-[2-(3,4,5-trimethoxy-phenoxy)-ethyl]-piperazine;

1-(4-Amino-2,3,5-trimethyl-phenoxy)-3-{4-[6,6-bis-(4-fluoro-phenyl)-hexyl]-piperazin-1-yl}-propan-2-ol;

1-[4-[3-(4-Amino-2,3,5-trimethyl-phenoxy)-2-hydroxy-propyl]-piperazin-1-yl]-6,6-bis-(4-fluoro-phenyl)-hexan-1-one;

1-(4-Benzothiazol-2-yl-piperazin-1-yl)-6,6-bis-(4-fluoro-phenyl)-hexan-1-one;

1-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-4-(3,5-bis-trifluoromethyl-benzyl)-piperazine;

1-[4-(3,5-Bis-trifluoromethyl-benzoyl)-piperazin-1-yl]-6,6-bis-(4-fluoro-phenyl)-hexan-1-one;

1-[4-(4-tert-Butyl-benzoyl)-piperazin-1-yl]-6,6-bis-(4-fluoro-phenyl)-hexan-1-one;

1-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-4-(4-bromo-benzyl)-piperazine;

2-(2-{4-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-piperazin-1-yl}-ethylsulfanyl)-benzothiazole;

6,6-Bis-(4-fluoro-phenyl)-1-[4-(4-hydroxy-3,5-dimethoxy-benzoyl)-piperazin-1-yl]-hexan-1-one;

4-{4-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-piperazin-1-ylmethyl}-2,6-dibromo-phenol;

1-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-4-(4-trifluoromethoxy-benzyl)-piperazine;

(2-{4-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-piperazin-1-yl}-ethyl)-(3,4,5-trimethoxy-benzyl)-amine;

1-{4-[2-(4-Fluoro-phenoxy)-ethyl]-piperazin-1-yl}-6,6-bis-(4-fluoro-phenyl)-hexan-1-one;

6,6-Bis-(4-fluoro-phenyl)-1-[4-(2-phenylamino-ethyl)-piperazin-1-yl]-hexan-1-one;
1-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-4-[2-(2,4-difluoro-phenoxy)-ethyl]-piperazine;
N-(2-{4-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-piperazin-1-yl}-2-oxo-ethyl)-benzamide;
N-(2-{4-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-piperazin-1-yl}-2-oxo-ethyl)-4-chloro-
benzamide;

N-(2-{4-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-piperazin-1-yl}-2-oxo-ethyl)-4-methyl-
benzamide;

N-(2-{4-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-piperazin-1-yl}-2-oxo-ethyl)-4-isopropyl-
benzamide;

N-(2-{4-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-piperazin-1-yl}-2-oxo-ethyl)-4-tert-butyl-
benzamide;

N-(2-{4-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-piperazin-1-yl}-2-oxo-ethyl)-4-fluoro-
benzamide;

N-(2-{4-[6,6-Bis-(4-fluoro-phenyl)-hexanoyl]-piperazin-1-yl}-2-oxo-ethyl)-benzamide;

N-(2-{4-[6,6-Bis-(4-fluoro-phenyl)-hexanoyl]-piperazin-1-yl}-2-oxo-ethyl)-4-chloro-
benzamide;

N-(2-{4-[6,6-Bis-(4-fluoro-phenyl)-hexanoyl]-piperazin-1-yl}-2-oxo-ethyl)-4-methyl-
benzamide;

N-(2-{4-[6,6-Bis-(4-fluoro-phenyl)-hexanoyl]-piperazin-1-yl}-2-oxo-ethyl)-4-isopropyl-
benzamide;

N-(2-{4-[6,6-Bis-(4-fluoro-phenyl)-hexanoyl]-piperazin-1-yl}-2-oxo-ethyl)-4-tert-butyl-
benzamide;

N-(2-{4-[6,6-Bis-(4-fluoro-phenyl)-hexanoyl]-piperazin-1-yl}-2-oxo-ethyl)-4-fluoro-
benzamide;

1-[4-(2-Benzylamino-ethyl)-piperazin-1-yl]-6,6-bis-(4-fluoro-phenyl)-hexan-1-one;

1-{4-[2-(4-Chloro-benzylamino)-ethyl]-piperazin-1-yl}-6,6-bis-(4-fluoro-phenyl)-
hexan-1-one;

6,6-Bis-(4-fluoro-phenyl)-1-{4-[2-(4-methyl-benzylamino)-ethyl]-piperazin-1-yl}-
hexan-1-one;

6,6-Bis-(4-fluoro-phenyl)-1-{4-[2-(4-isopropyl-benzylamino)-ethyl]-piperazin-1-yl}-hexan-1-one;

1-{4-[2-(4-tert-Butyl-benzylamino)-ethyl]-piperazin-1-yl}-6,6-bis-(4-fluoro-phenyl)-hexan-1-one;

1-{4-[2-(4-Fluoro-benzylamino)-ethyl]-piperazin-1-yl}-6,6-bis-(4-fluoro-phenyl)-hexan-1-one;

6,6-Bis-(4-fluoro-phenyl)-1-[4-(1-hydroxy-pyridine-4-carbonyl)-piperazin-1-yl]-hexan-1-one;

4-{4-[6,6-Bis-(4-fluoro-phenyl)-hexyl]-piperazin-1-ylmethyl}-2,6-dimethoxy-phenol;

9,9-Diphenyl-1-[4-(3,4,5-trimethoxy-benzyl)-piperazin-1-yl]-nonan-1-one;

1-[4-(3,5-Di-tert-butyl-4-methoxy-benzoyl)-2-methyl-piperazin-1-yl]-6,6-bis-(4-fluoro-phenyl)-hexan-1-one;

1-[4-(3,5-Di-tert-butyl-4-methoxy-benzoyl)-3-methyl-piperazin-1-yl]-6,6-bis-(4-fluoro-phenyl)-hexan-1-one;

1-[4-(3,5-Di-tert-butyl-benzoyl)-2-methyl-piperazin-1-yl]-6,6-bis-(4-fluoro-phenyl)-hexan-1-one; and

1-[4-(4-tert-Butyl-benzoyl)-2-methyl-piperazin-1-yl]-6,6-bis-(4-fluoro-phenyl)-hexan-1-one, including the pharmaceutically acceptable salts thereof.

30. (previously presented): A pharmaceutical composition which comprises, in admixture with a pharmaceutically acceptable excipient, a unit dosage amount of at least one compound of claim 19.

31. (previously presented): A pharmaceutical composition which comprises, in admixture with a pharmaceutically acceptable excipient, a unit dosage amount of at least one compound of claim 29.